REMARKS

Applicant notes with appreciation the opportunity to discuss the above-referenced application in the course of a personal interview that occurred on 26 March 2003. With this amendment independent claim 1 remains pending, as well as the claims dependent therefrom. Support for the amendments to the claims is found throughout the application as filed. As a result, it is respectfully submitted that no new matter has been added to the above-referenced application by way of this amendment.

Claims 1-11 currently stand rejected under 35 U.S.C. §112, first paragraph. Claims 1-11 also stand rejected under 35 U.S.C. §112, second paragraph. Lastly, claims 1-11 stand rejected as being obvious over Amidon et al. (U.S. Patent 5,834,022) in view of Woo (U.S. Patent 5,589,455) and Gennaro et al. (Remington's Pharmaceutical Sciences, 18th Edition, 1990, pp. 1662-1664).

Remarks Directed to Rejection of Pending Claims Under 35 U.S.C. §112, First Paragraph

The pending claims stand rejected hereunder as lacking criteria that define drugs operative with the instant invention. The rejection is also based on the lack of information allowing a skilled artisan to ascertain drugs operative within the present invention without undue experimentation. (Paper No. 14, page 3, first full paragraph).

Applicant submits that the prior art reference already of record Gennaro et al. (Remington's Pharmaceutical Sciences) as prior art available to a skilled artisan at the time the invention was made would readily appreciate that a "poorly soluble drug" as detailed in claim 1 at line 8 and in claim 12 at line 5 has a specific meaning in the art. Gennaro et al. Vol. 20, a later volume of the same work as cited by the Examiner, details at Table 16-1

descriptive terms for solubility where "practically insoluble, or insoluble denotes more than 10,000 parts of solvent for one part of solute."

The instant specification at page 9, line 17 – page 10, line 6 is submitted to teach one skilled in the art that the invention pertains to the solubilization of an insoluble drug per amended independent claim 1. This teaching within the specification coupled with the known meaning of insoluble as indicating more than 10,000 parts solvent for one part of solute drug. As a result, Applicant submits that independent claim 1 and those claims that depend therefrom in amended form clearly define a drug according to the pending claims. It is further submitted that one skilled in the art with a knowledge of the commonly held definition of an insoluble drug could readily ascertain drugs operative within the present invention absent experimentation and solely through available tabular solubility data for a potential drug candidate to be used with the present invention.

In light of the above amendments and remarks, it is now believed that the rejection of pending claims 1-11 under 35 U.S.C. §112, first paragraph, is no longer proper. Withdrawal of the rejection of claims 1-11 under 35 U.S.C. §112, first paragraph, is hereby solicited.

Remarks Directed to Rejection of Pending Claims 1-11 Under 35 U.S.C. §112, Second Paragraph

The expression "maintaining a region adjacent to said drug particle that contains solubilizing agent micelles to solubilize same . . ." is considered to render independent claim 1 indefinite as to the region encompassed and secondly, as to what the word "same" refers.

Independent claim 1 has been amended such that the phrase in question (claim 1, lines 15-16) now recites "maintaining adjacent to said drug particle solubilizing agent micelles to solubilize said drug . . . ". It is believed that this amendment, by deleting the phrase a

"region", makes clear that solubilizing agent micelles are present directly adjacent to the drug particle and serve to solubilize the drug from the drug particle.

It is also stated in the Office Action that "the variables in the equation recited in the claims [claim 1] have no units. One of ordinary skill in the art would consider the units of these variables critical to the invention." (Paper No. 14, page 4). Applicant submits that the ability to perform unit analysis to determine if the resulting ratio of drug particle mass, M_P to the volume of the diffusional boundary layer, V_{BL} does in fact have the correct units. Applicant submits that one skilled in the art would readily appreciate that the Greek symbol δ, which is the thickness of the diffusional boundary layer, necessarily has units of linear dimension (e.g. micron, millimeter, centimeter, inch, etc.). Additionally, surface area, SA, is well known to one skilled in the art to have units of linear dimension raised to the second power. The diffusion coefficient D is defined within the specification consistent with the definition given in the prior art of record Gennaro et al. to have dimensions of linear dimension squared per unit time. By way of example, assuming all linear dimensions are in units of centimeters and all units of time are in units of seconds, results in a change of mass as a function of time in units of seconds per centimeters cubed. In light of the above remarks, Applicant respectfully submits that one skilled in the art would readily appreciate through a unit analysis of the equation shown in claim 1, a suitable set of units upon inserting variables into the claimed equation with appropriate conversion factors to obtain the stated inventive ratio in preselected units of time and volume. As such, Applicant respectfully submits that units of the variables relevant to the equations found in independent claim 1 are immaterial so long as a unit analysis is performed on the expression and unit analysis is well within the purview of one skilled in the art.

Lastly, the pending claims are deemed to be indefinite because of the expression found in independent claim 1 that "drug disposed in the drug particle has a solubility greater than twofold that of said drug in a bulk form . . .". In response to this rejection, Applicant has amended independent claim 1 to emphasize the fact that the solubility increase is at least two times that compared with a large drug particle having orders of magnitude larger than the inventive drug particle. Namely, that the solubility of twofold greater compared to the same drug in a "bulk powder form". Support for this amendment is found in Figure 4 and the related specification text as filed. Applicant submits that independent claim 1 now recites that a drug particle satisfying the equation recited in that claim and having the corresponding solubilizing agent micelles adjacent to the drug particle has at least a twofold increase in drug solubility relative to the solubility associated with a bulk drug tablet and that one of ordinary skill in the art can readily appreciate the nature of the comparison.

In light of the above amendments and remarks, the rejection of claims 1-11 under 35 U.S.C. §112, second paragraph, is believed to no longer be proper. Withdrawal of the rejection of claims 1-11 under 35 U.S.C. §112, second paragraph, is solicited.

Remarks Directed to Rejection of Pending Claims Under 35 U.S.C. §103(a)

Pending claims 1-11 stand rejected under 35 U.S.C. §103(a) over Amidon et al. in view of Woo and Gennaro et al. Amidon et al. is cited for teaching a coating composition of gelatin and lecithin with a drug particle therein. Amidon et al. is also cited as teaching increasing the dissolution rates of both cyclosporin and griseofulvin 20 and 40 percent respectively using the gelatin/lecithin coating detailed therein.

Amidon et al. is cited as lacking a teaching as to the coating composition containing emulsion, microemulsion or micelles, as well as the matrix forming the boundary layer being a film.

Woo is cited to bolster the teaching of Amidon et al. with respect to a microemulsion being used in soft capsule pharmaceutical formulation to enhance the solubility of a poorly soluble drug, such as cyclosporin.

Gennaro et al. is cited for teaching the use of gelatin film in the preparation of soft gelatin capsules. (Paper No. 14, pp. 5-6).

Applicant submits that the pending claims represent a surprising result relative to the prior art combination of record. In addition, the pending claims include limitations that must be considered especially in light of the fact that these limitations are lacking in the prior art.

Independent claim 1 teaches a ratio of the initial mass of a drug particle relative to the volume of the diffusional boundary layer made up of the matrix and solubilizing agent. The satisfaction of this relationship (claim 1, line 10) defines the quantity of drug relative to matrix and solubilizing agent substances. As Figures 3 and 4 make clear, satisfying this relationship yields increases in dissolution rate greater than twofold compared to bulk powder (Figure 3) or the diffusional boundary layer components separately (Figure 4). Applicant readily concedes that Amidon et al. teaches the coating of a poorly soluble drug particle with a gelatin/lecithin mixture, as well as a broad concentration range between gelatin and lecithin (Amidon et al. column 3, lines 42-47). However, Amidon et al. is silent as to the relative dimensions of the core drug particle and the surrounding diffusional boundary layer. Additionally, Amidon et al. is silent as to the presence of surfactant micelles in the boundary region. Amidon et al. is respectfully submitted to lack a teaching as to controlling the parameters of the boundary layer as a means for increasing the dissolution rate of insoluble drugs.

Neither Woo nor Gennaro et al. bolsters the teaching of Amidon et al. with respect to boundary layer control parameters.

As none of the prior art references alone or in combination recognizes such a relationship, Applicant submits that the pending claims in amended form are nonobvious over the prior art combination of record. Withdrawal of the rejection of claims 1-11 under 35 U.S.C. §103(a) is solicited.

Summary

Claims 1-11 are the claims pending in this application. Each claim is now believed to be in proper form and directed to allowable and patentable subject matter. Reconsideration and allowance of the claims is solicited. If the Examiner finds to the contrary, it is respectfully requested that the undersigned in charge of this application be called at the telephone number given below in order to resolve any remaining issues.

Respectfully submitted,

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Janice R. Kuehn